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Dose-years as an improved index of cumulative tobacco smoke exposure

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Summary In assessing the link between tobacco smoking and disease, it is important to determine long-term, cumulative exposure to tobacco smoke as accurately as possible. Conventional methods of assessing exposure to tobacco smoke each have intrinsic limitations. Self-reporting of tobacco use, and the conversion of this data to pack-years, can be prone to error due to individuals wishing to conceal smoking habits, inaccurate reporting of daily cigarette consumptions or years of smoking, and failure to take into account the variation that exists in inter-individual smoking experiences. Measurement of cotinine, a major metabolite of nicotine in humans, is a reliable method of monitoring recent doses of tobacco smoke exposure. Cotinine concentrations, however, may remain stable in smokers over the longer term. Therefore, dose-years, and more specifically cotinine-years, may represent an improved index of cumulative tobacco smoke exposure. © 2001 Harcourt Publishers Ltd

BACKGROUND

In epidemiological studies, the accurate estimation of cumulative tobacco smoke exposure is essential in order to accurately assess the link between smoking and smoking-related, or potentially smoking-related, diseases. Exposure to tobacco smoke is conventionally measured by several simple methods, each with intrinsic limitations. Self-reports of number of cigarettes smoked provide only a limited index of cumulative tobacco smoke exposure when described as pack-years (1 pack-year is the exposure that corresponds to smoking one pack of 20 cigarettes per day for 1 year) and weighted pack-years (allowing for hand-rolled cigarette consumption, cigar smoking and pipe smoking). Recently, estimations of environmental tobacco smoke (ETS) pack-years have been attempted, where one ETS pack-year is the exposure within a confined space to ETS produced by an active smoker consuming one pack of 20 cigarettes per day for 1 year. Similarly, an exposure index has been employed where cumulative ETS exposure is estimated as years of ETS exposure multiplied by the average duration of daily exposure to ETS. The major limitations of pack-years as an index of cumulative exposure include inaccurate and/or false reporting of smoking habits and the fact that the number of cigarettes smoked does not take account of the considerable inter-individual variation in mode of smoking. Even when a group of individuals all smoke a similar number of cigarettes per day, differences in the type of cigarette smoked, the frequency and depth of inhalation, and the amount of stub left will all contribute to wide variation in actual exposure to cigarette smoke.

Biochemical markers of tobacco smoke exposure include expired-air carbon monoxide, blood carboxyhaemoglobin, and thiocyanate, cotinine, or nicotine in serum, plasma, urine or saliva (1). Of these, cotinine is commonly regarded as the gold standard. A circulating cotinine concentration of 15 ng ml^{-1} is typically employed to differentiate smokers and non-smokers. While all these markers allow accurate assessment of current or recent smoke exposure, their half-lives are short (h to days). Therefore, in epidemiological studies, biochemical analysis of tobacco smoke constituents or metabolites is

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traditionally utilized to confirm current smoking status, if used at all, and not to provide data on longterm smoke exposure.

HYPOTHESIS

Dose-years represent an improved index of cumulative tobacco smoke exposure compared to the conventional index of pack-years. Importantly, there is evidence to suggest that serum cotinine concentrations do not vary significantly over a period of 12 months in individual smokers (2). Since serum and saliva cotinine concentrations are highly correlated, the same will be true of saliva cotinine levels. Additionally, some studies have been able to show significant associations between cotinine levels and disease that are not apparent using reported cigarette consumption to describe smoking habits (2,3). Measurement of cotinine in body fluids is sensitive enough to detect and quantify passive smoking, allowing comparisons of total smoke exposure (active smoking and ETS-exposure). In addition, cotinine measurements allow an accurate estimate of recent smoke intake that reflects individual variation in smoking habits (2,4–6). Therefore, cotinine would seem to represent a better marker from which to base a cumulative score of tobacco smoke exposure than self-reported consumption. While cotinine-years will still rely on anamnestic data to describe duration of smoking, this problem is unavoidable.

Consider 20 smokers who report to have smoked one pack of 20 cigarettes per day for 20 years. Using the conventional approach, such a population would be described as having a mean cumulative tobacco smoke exposure of 20 pack-years, with a standard deviation of 0.0. Cotinine-years, however, would reflect the variation in cumulative smoke intake in the same population, with the standard deviation determined by the range in cotinine levels. Large variations in the cotinine concentrations of smokers reporting the same daily cigarette consumption have been reported by several workers (2,4,5). In a recent study we reported that two smoking subjects representing the extreme values in the range of cotinine concentrations detected in a group of smokers (83 to 688 ng ml^{-1}), both reported that they smoked 20 cigarettes per day (6). Cotinine-years, therefore, permit incorporation of individual variability in smoking habits into an index of cumulative exposure that pack-years cannot.

CONCLUDING REMARKS

Cotinine concentrations in body fluids are usually reported as ng ml^{-1} or nmol L^{-1}. However, as the serum cotinine concentration in smokers may reach 1000 ng ml^{-1} (2), it may be preferable to use a larger unit to describe cotinine concentration, such as μg ml^{-1} cotinine, for the purpose of establishing cotinine-years.

Studies that aim to assess the value of cotinine-years in epidemiological research may be warranted. Such studies could include re-analysis of reports already in the medical literature that have examined the relations between smoking and a wide variety of health outcome measures using conventional pack-years as the index of cumulative tobacco smoke exposure, but where biochemical methods were also utilized in order to validate current smoking status (7–10). Studies to confirm the stability of serum cotinine concentration in individual smokers over 1 year (2), and longer periods, would be a critical step in validation of cotinine-years as a reliable index of cumulative tobacco smoke exposure.

An improved index of cumulative tobacco smoke exposure should be of use in more accurately establishing the relationship between smoking and smoking-associated diseases, or potentially smoking-related diseases. This may, in turn, provide information that might prove useful in the implementation of legislative and social anti-tobacco prevention strategies.

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